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Sculpted light and matter for nanobiophotonics and two-photon optogenetics

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The synergy between nanotechnology, biotechnology and photonics is spawning the emerging fields of nano-biotechnology and nano-biophotonics. Photonic innovations already hurdle the diffraction barrier for imaging with nanoscopic resolutions. However, scientific hypothesis testing demands tools, not only for observing nanoscopic phenomena, but also for *reaching into and manipulating* nanoscale constituents in this domain. This conribution is two-fold desribing the new use of proprietary strongholds we currently are establishing at DTU Fotonik on new means of *sculpting* of both light and matter for bio-probing at the smallest scales.

Recently featured in Nature Photonics the authors promoted the idea of fabricating a new class of so-called Topology Optimised microstructures via two-photon polymerization (2PP) and pioneering their use in “nanobio-robotics” to interact with and probe reconfigurable micro-environments. In this new undertaking the aim is to combine 2PP micro-fabrication and optical manipulation to demonstrate a structure-mediated micro-to-nano coupling paradigm for controlled manipulation of subdiffraction-limited nano-tools. The three-dimensional structures and resolution realizable in 2PP light-fabrication can already today create nano-tools fused into larger microstructures that, in turn, are steerable by dynamic light beams that are oblivious to the diffraction barrier. Applying multiple independently controllable beam traps on these microstructures using our proprietary BioPhotonics Workstation platform enables real-time “light robotic” manipulation with six degrees of freedom. This sets the stage for advanced studies using calibrated steering of optimally shaped and functionalized tools for biophotonics at the cellular level not available at the scientific arena as of today.

Two-photon spatio-temporal light engineering can also be used to expand the microscopic imaging modalities available to assist this light-driven nano-manipulation approach. Featured in a recent issue of Nature Methods we were pioneering research in neuro-photonics and optogenetics highly useful for future biophotonics undertakings on the smallest cellular scales. This research promises a powerful approach for controlling light-gated ion channels and pumps that makes it possible to probe intact neural circuits by manipulating the activity of groups of genetically similar neurons. This makes it possible to precisely aim space-time sculpted light at single neuronal processes, neurons or groups of neurons. The underlying light-engineering is currently being scientifically refined in a strong international context to address - for the first time - arbitrary and speckle-free ‘4D’ spatial and temporal two-photon light-sculpting.

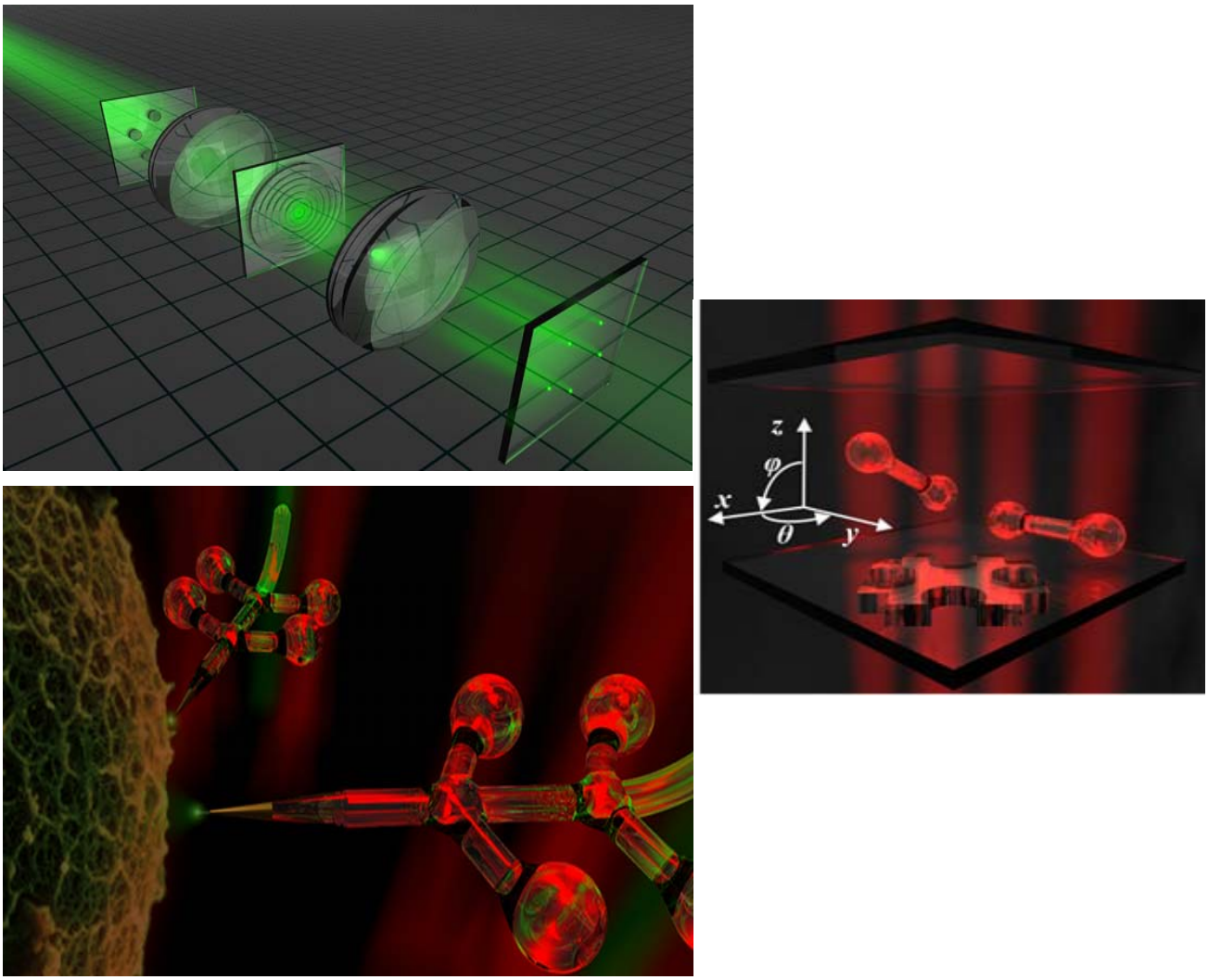

Figure 1: Proprietrary 3D light sculpting, 3D light manipulation and 3D nanobio-sensing. Adapted from refs [1-7].

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